

X16339\_US  
SEQUENCE LISTING

<110> Eli Lilly and Company  
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Kikly, Kristine K  
Manetta, Joseph V  
Witcher, Derrick R

<120> Anti-Ghrelin Antibodies

<130> X-16339\_US

<150> PCT/US2004/025604

<151> 2004-09-02

<150> 60/582111

<151> 2004-06-23

<160> 37

<170> PatentIn version 3.3

<210> 1

<211> 339

<212> DNA

<213> Mus sp.

<220>

<221> misc\_feature

<222> (1)..(339)

<223> Polynucleotide sequence encoding 1181 light chain variable region

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atctcttgca gatctagtca gagccttgta cacagtaatg gaaacaccta tttacattgg	120
tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt	180
tctgggggtcc cagacagggt cagtggcagt ggatcagggga cagatttcac actcaagatc	240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg	300
tacacgttcg gagggggggac caagctggaa ataaaacgg	339

<210> 2

<211> 339

<212> DNA

<213> Mus sp.

<220>

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<222> (1)..(339)

<223> Polynucleotide sequence encoding 1621 light chain variable region

<400> 2

gatgttgatgc tgacccaaac tccactctcc ctgcctgtca gtcttgagaga tcaagcctcc	60
atctcttgca gatctagtca gagccttgta cacagtaatg gaagcaccta tttacattgg	120
tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt	180
tctgggggtcc cagacagggt cagtggcagt ggatcagggga cagatttcac actcaagatc	240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg	300

tacacgttcg gaggggggac caagctggaa ataagacgg

339

<210> 3  
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<220>  
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 <222> (1)..(113)  
 <223> 1181 light chain variable region amino acid sequence

<400> 3

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly  
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
 20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
 35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro  
 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile  
 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser  
 85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
 100 105 110

Arg

<210> 4  
 <211> 113  
 <212> PRT  
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<220>  
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 <222> (1)..(113)  
 <223> 1621 light chain variable region amino acid sequence

<400> 4

Asp Val Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly  
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
 20 25 30

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Asn Gly Ser Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro  
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile  
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser  
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

Arg

<210> 5  
<211> 16  
<212> PRT  
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<220>  
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<222> (1)..(16)  
<223> 1181 light chain CDR1 amino acid sequence

<400> 5

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His  
1 5 10 15

<210> 6  
<211> 16  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE  
<222> (1)..(16)  
<223> 1621 light chain CDR1 amino acid sequence

<400> 6

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Ser Thr Tyr Leu His  
1 5 10 15

<210> 7  
<211> 16  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE

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<222> (1)..(16)  
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<220>  
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 <222> (12)..(12)  
 <223> Xaa is selected from the group consisting of Gly (G), Ala (A), Ser (S), Thr (T), Cys (C), Asn (N) and Gln (Q)

<400> 7

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Xaa Thr Tyr Leu His  
 1 5 10 15

<210> 8  
 <211> 7  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(7)  
 <223> 1181 and 1621 light chain CDR2 amino acid sequence

<400> 8

Lys Val Ser Asn Arg Phe Ser  
 1 5

<210> 9  
 <211> 9  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(9)  
 <223> 1181 and 1621 light chain CDR3 amino acid sequence

<400> 9

Ser Gln Ser Thr His Val Pro Tyr Thr  
 1 5

<210> 10  
 <211> 357  
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 <223> Polynucleotide sequence encoding 1181 heavy chain variable region

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 tcctgcacag cttctggcct caacattaaa gactacttta tgcagtgggt gaagcagagg 120  
 cctgaacagg gcctggagtg gattggatgg attgatcctg agaatgggtga aactggatat 180  
 gccccgaagt tccagggcaa ggccactatg actgcagaca cagcctccaa tacagcctac 240

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ctgcaactca gcagcctgac atctgaggac actgccctgt attactgtaa tgcaccttcg      300
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<210> 11
<211> 357
<212> DNA
<213> Mus sp.
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<223> Polynucleotide sequence encoding 1621 heavy chain variable region
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caggtccagc tgcagcagtc tggggcagag cttgtgaggt caggggcctc agtcaagttg      60
tcctgcacag cttctggctt caacattaaa gactactttg tgcagtgggt gaagcagagg      120
cctgaacagg gcctggagtg gattggatgg attgatcctg agaatgggtga aactggatat      180
gccccgaagt tccagggcaa ggccactatg actgcagaca cagcctccaa tacagcctac      240
ctgcaactca gcagcctgac atctgaggac actgccctgt atttctgtaa tgcaccttcg      300
gtagtggcta aatacttcga tgtctggggc gcagggacca cggtcaccgt ctcctca      357
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<210> 12
<211> 119
<212> PRT
<213> Mus sp.
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<220>
<221> MISC_FEATURE
<222> (1)..(119)
<223> 1181 heavy chain amino acid sequence
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<400> 12
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Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Ser Gly Ala
1          5          10          15
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Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Tyr
20        25        30
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```
Phe Met Gln Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Ile
35        40        45
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```
Gly Trp Ile Asp Pro Glu Asn Gly Glu Thr Gly Tyr Ala Pro Lys Phe
50        55        60
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```
Gln Gly Lys Ala Thr Met Thr Ala Asp Thr Ala Ser Asn Thr Ala Tyr
65        70        75        80
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Leu Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Leu Tyr Tyr Cys
85        90        95
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Asn Ala Pro Ser Val Val Ala Lys Tyr Phe Asp Val Trp Gly Ala Gly  
 100 105 110

Thr Thr Val Thr Val Ser Ser  
 115

<210> 13  
 <211> 118  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(118)  
 <223> 1621 heavy chain amino acid sequence

<400> 13

Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Ser Gly Ala  
 1 5 10 15

Ser Val Lys Leu Ser Cys Thr Ala Ser Gly Phe Asn Ile Lys Asp Tyr  
 20 25 30

Phe Val Gln Trp Val Lys Gln Arg Pro Glu Gln Gly Leu Glu Trp Gly  
 35 40 45

Trp Ile Asp Pro Glu Asn Gly Glu Thr Gly Tyr Ala Pro Lys Phe Gln  
 50 55 60

Gly Lys Ala Thr Met Thr Ala Asp Thr Ala Ser Asn Thr Ala Tyr Leu  
 65 70 75 80

Gln Leu Ser Ser Leu Thr Ser Glu Asp Thr Ala Leu Tyr Phe Cys Asn  
 85 90 95

Ala Pro Ser Val Val Ala Lys Tyr Phe Asp Val Trp Gly Ala Gly Thr  
 100 105 110

Thr Val Thr Val Ser Ser  
 115

<210> 14  
 <211> 10  
 <212> PRT  
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 <223> 1181 heavy chain CDR1 amino acid sequence

<400> 14

Gly Phe Asn Ile Lys Asp Tyr Phe Met Gln  
 1 5 10

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<210> 15  
 <211> 10  
 <212> PRT  
 <213> Mus sp.

<220>  
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 <222> (1)..(10)  
 <223> 1621 heavy chain CDR1 amino acid sequence

<400> 15

Gly Phe Asn Ile Lys Asp Tyr Phe Val Gln  
 1 5 10

<210> 16  
 <211> 10  
 <212> PRT  
 <213> Mus sp.

<220>  
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 <223> Heavy chain CDR1 amino acid sequence (generic for 1181 and 1621)

<220>  
 <221> MISC\_FEATURE  
 <222> (9)..(9)  
 <223> Xaa is a hydrophobic amino acid selected from the group  
 consisting of Val (V), Leu (L), Ile (I), Met (M), and Pro (P)

<400> 16

Gly Phe Asn Ile Lys Asp Tyr Phe Xaa Gln  
 1 5 10

<210> 17  
 <211> 17  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(17)  
 <223> 1181 and 1621 heavy chain CDR2 amino acid sequence

<400> 17

Trp Ile Asp Pro Glu Asn Gly Glu Thr Gly Tyr Ala Pro Lys Phe Gln  
 1 5 10 15

Gly

<210> 18  
 <211> 10  
 <212> PRT  
 <213> Mus sp.

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<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(10)  
 <223> 1181 and 1621 heavy chain CDR3 amino acid sequence

<400> 18

Pro Ser Val Val Ala Lys Tyr Phe Asp Val  
 1 5 10

<210> 19  
 <211> 28  
 <212> PRT  
 <213> Homo sapiens

<220>  
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 <222> (1)..(28)  
 <223> Human ghrelin amino acid sequence

<220>  
 <221> MISC\_FEATURE  
 <222> (28)..(28)  
 <223> Xaa is Arg or absent

<400> 19

Gly Ser Ser Phe Leu Ser Pro Glu His Gln Arg Val Gln Gln Arg Lys  
 1 5 10 15

Glu Ser Lys Lys Pro Pro Ala Lys Leu Gln Pro Xaa  
 20 25

<210> 20  
 <211> 16  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(16)  
 <223> 4641 light chain CDR1 amino acid sequence

<400> 20

Arg Ser Ser Gln Ser Leu Val His Ser Asp Gly Asn Thr Tyr Leu Asp  
 1 5 10 15

<210> 21  
 <211> 9  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(9)  
 <223> 4641 light chain CDR3 amino acid sequence

<400> 21



Ser Gln Ser Thr Tyr Val Ser Tyr Thr  
1 5

<210> 22  
<211> 16  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE  
<222> (1)..(16)  
<223> 1451 light chain CDR1 amino acid sequence

<400> 22

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His  
1 5 10 15

<210> 23  
<211> 9  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE  
<222> (1)..(9)  
<223> 1451 light chain CDR3 amino acid sequence

<400> 23

Ser Gln Ser Thr Leu Val Pro Tyr Thr  
1 5

<210> 24  
<211> 10  
<212> PRT  
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<223> 4641 and 1451 heavy chain CDR1 amino acid sequence

<400> 24

Ala Tyr Thr Phe Thr Thr Tyr Trp Met His  
1 5 10

<210> 25  
<211> 17  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE  
<222> (1)..(17)  
<223> 4641 heavy chain CDR2 amino acid sequence

<400> 25

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Met	Ile	Asp	Pro	Ser	Asn	Ser	Asp	Thr	Trp	Leu	Asn	Gln	Lys	Phe	Lys
1				5					10					15	

Asp

<210> 26  
 <211> 17  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(17)  
 <223> 1451 heavy chain CDR2 amino acid sequence

<400> 26

Met	Ile	Asp	Pro	Tyr	Asn	Ser	Glu	Thr	Trp	Leu	Asn	Gln	Lys	Phe	Lys
1				5					10					15	

Asp

<210> 27  
 <211> 5  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(5)  
 <223> 4641 and 1451 heavy chain CDR3 amino acid sequence

<400> 27

Thr	Gly	Phe	Asp	Tyr
1				5

<210> 28  
 <211> 16  
 <212> PRT  
 <213> Mus sp.

<220>  
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 <222> (1)..(16)  
 <223> Light chain (generic for 4641, 1451, 1181, and 1621) CDR1 amino acid sequence

<220>  
 <221> MISC\_FEATURE  
 <222> (10)..(10)  
 <223> Xaa is selected from the group consisting of Asn (N) and Asp (D)

<220>  
 <221> MISC\_FEATURE  
 <222> (12)..(12)  
 <223> Xaa is selected from the group consisting of Gly (G), Ala (A), Ser (S), Thr (T), Cys (C), Asn (N) and Gln (Q)

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<220>  
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 <222> (16)..(16)  
 <223> Xaa is selected from the group consisting of His (H) and Asp (D)  
 <400> 28

Arg Ser Ser Gln Ser Leu Val His Ser Xaa Gly Xaa Thr Tyr Leu Xaa  
 1 5 10 15

<210> 29  
 <211> 9  
 <212> PRT  
 <213> Mus sp.

<220>  
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 <222> (1)..(9)  
 <223> Light chain (generic for 4641, 1451, 1181 and 1621) CDR3 amino acid sequence

<220>  
 <221> MISC\_FEATURE  
 <222> (5)..(5)  
 <223> Xaa is selected from the group consisting of His (H), Tyr (Y), and Leu (L)

<220>  
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 <222> (7)..(7)  
 <223> Xaa is selected from the group consisting of Pro (P), Ser (S), and Thr (T)

<400> 29  
 Ser Gln Ser Thr Xaa Val Xaa Tyr Thr  
 1 5

<210> 30  
 <211> 113  
 <212> PRT  
 <213> Mus sp.

<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(113)  
 <223> 4641 light chain variable region amino acid sequence

<400> 30  
 Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly  
 1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
 20 25 30

Asp Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
 35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro  
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55

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile  
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser  
85 90 95

Thr Tyr Val Ser Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

Arg

<210> 31  
<211> 113  
<212> PRT  
<213> Mus sp.

<220>  
<221> MISC\_FEATURE  
<222> (1)..(113)  
<223> 1451 light chain variable region amino acid sequence  
<400> 31

Asp Val Val Leu Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly  
1 5 10 15

Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser  
20 25 30

Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser  
35 40 45

Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro  
50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile  
65 70 75 80

Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser  
85 90 95

Thr His Val Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys  
100 105 110

Arg

<210> 32  
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<220>  
 <221> MISC\_FEATURE  
 <222> (1)..(114)  
 <223> 4641 heavy chain variable region amino acid sequence

<400> 32

Gln Val Gln Leu Gln Gln Ser Arg Pro Glu Leu Val Arg Pro Gly Ala  
 1 5 10 15

Ser Val Lys Met Ser Cys Arg Ala Ser Ala Tyr Thr Phe Thr Thr Tyr  
 20 25 30

Trp Met His Trp Val Arg Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

Gly Met Ile Asp Pro Ser Asn Ser Asp Thr Trp Leu Asn Gln Lys Phe  
 50 55 60

Lys Asp Lys Ala Thr Leu Asn Val Asp Arg Ser Ser Asn Thr Ala Tyr  
 65 70 75 80

Met Gln Leu Thr Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
 85 90 95

Ala Arg Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val  
 100 105 110

Ser Ser

<210> 33  
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 <212> PRT  
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 <221> MISC\_FEATURE  
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<400> 33

Gln Val His Val Lys Gln Ser Gly Pro Glu Leu Val Arg Pro Gly Ala  
 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Ala Tyr Thr Phe Thr Thr Tyr  
 20 25 30

Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile  
 35 40 45

Gly Met Ile Asp Pro Tyr Asn Ser Glu Thr Trp Leu Asn Gln Lys Phe  
 50 55 60

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Lys Asp Lys Ala Thr Leu Asn Val Asp Arg Ser Ser Asn Thr Ala Tyr  
65 70 75 80

Met Lys Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg Thr Gly Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu Thr Val  
100 105 110

Ser Ser

<210> 34  
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<212> DNA  
<213> Mus sp.

<220>  
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<223> 1451 LCVR polynucleotide

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aacacctatt tacattggtg cctgcagaag ccaggccagt ctccaaagct cctgatctac 180  
aaagtttcca accgattttc tgggggtcca gacagggttca gtggcagtgg atcagggaca 240  
gatttcacac tcaagatcag cagagtggag gctgaggatc tgggagttta tttctgctct 300  
caaagtacac atgttccgta cacgttcggt ggaggcacca agctggaaat caaacgggct 360  
gatgcttcac caactgta 378

<210> 35  
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<212> DNA  
<213> Mus sp.

<220>  
<221> misc\_feature  
<222> (1)..(360)  
<223> 1451 HCVR polynucleotide

<400> 35  
caggtccacg tgaagcagtc tgggcctgaa ctggtgaggc ctggggcttc agtgaagatg 60  
tcctgcaagg cttcagccta taccttcacc acctactgga tgcactgggt gaaacagagg 120  
cctggacaag gccttgagtg gattggcatg attgatcctt acaatagtga aacttggtta 180  
aatcagaaat tcaaggacaa ggccacattg aatgtagaca gatcctccaa cacagcctac 240  
atgaagctca gcagcctgac atctgaggac tctgcagtct attactgtgc aagaactggt 300  
tttgactact ggggccaagg caccactctc acagtctcct cagccaaaac gacaccccca 360

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<210> 36  
 <211> 378  
 <212> DNA  
 <213> Mus sp.

<220>  
 <221> misc\_feature  
 <222> (1)..(378)  
 <223> 4641 LCVR polynucleotide

<400> 36  
 tctactccag cttgggcaga tggtgtgatg acccaaactc cactctccct gcctgtcagt 60  
 cttggagatc aagcctccat ctcttcgaga tctagtcaga gccttgtaga cagtgtgga 120  
 aacacctatt tacattggtg cctgcagaag ccaggccagt ctccaaagct cctgatctac 180  
 aaagtttcca accgattttc tgggggtcca gacaggttca gtggcagtgg atcagggaca 240  
 gatttcacac tcaagatcag cagagtggag gctgaggatc tgggagttta tttctgctct 300  
 caaagtacat atgtttcgta cacgttcgga ggggggacca agctggaaat aaaacgggct 360  
 gatgctgcac caactgta 378

<210> 37  
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<220>  
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 <223> 4641 HCVR polynucleotide

<400> 37  
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 cctggacaag gccttgagtg gattggcatg attgatcctt ccaatagtga tacttggtta 180  
 aatcagaagt tcaaggacaa ggccacattg aatgtagaca gatcctccaa cacagcctac 240  
 atgcagctca ccagcctgac atctgaggac tctgcagtct attactgtgc aagaactggt 300  
 ttgactact ggggccaagg caccactctc acagtctcct cagccaaaac gacaccccca 360